

ASTHMA

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Objectives

- At the conclusion of the presentation, participants should be able to:
 - ID signs and symptoms consistent with asthma and allergic rhinitis
 - Differentiate the various severities of asthma
 - Summarize an appropriate treatment regimen for asthma of various severities

Allergic Rhinitis

- Symptoms: sneezing, itching, rhinorrhea, and congestion
- Nasal smear with $>10\%$ eosinophils suggestive
- Dx can be confirmed by allergen-specific Ig-E
- Classification
 - Persistent or intermediate
 - Graded relative to severity

Allergic Rhinitis

- Affects 15%-50% of world-wide population
- Affects 40 million people in the US
- Prevalence increasing (increasing airborne pollutants, rising dust mite populations, poor ventilation in buildings, increased time indoors by people and pets, dietary factors, changes in gut indigenous microflora, increased abx use, increasingly sedentary lifestyle?????????)

Allergic Rhinitis

- Associated with asthma
 - 95% of people with allergic asthma have rhinitis
 - 30% of people with allergic rhinitis have asthma (compared to 3-5% of general population)
 - Family history of atopy seems associated with progression of either allergic rhinitis or asthma to allergic rhinitis + asthma
 - Treatment of allergic rhinitis reduces ER visits for asthma

Management of Allergic Rhinitis

- Identification of allergens
 - Pollen
 - Molds/fungi
 - Dust mites
 - Animal dander
 - Cockroaches
- Avoid or minimize exposure to allergens
- Patient education

Management of Allergic Rhinitis

- Pharmacotherapy
 - Intra-nasal corticosteroids
 - Antihistamines (non-sedating preferred)
 - Not recommended to use sedating qhs and non-sedating qAM
 - Decongestants
 - Antihistamine/decongestant combinations
 - Mast cell stabilizers
 - Leukotriene antagonists

Management of Allergic Rhinitis

- Allergen Immunotherapy
 - Repeated, controlled administration of specific allergens to patients with IgE-mediated conditions
 - May impede progression of allergic rhinitis to asthma
 - May prevent multiple sensitizations and the need for prolonged/excessive use of pharmacotherapies
 - Consider when sx not controlled on medications

Definition of Asthma

- Chronic inflammatory disorder of the airways in which many cells and cellular elements play a role. In susceptible individuals, this inflammation causes recurrent episodes of wheezing, breathlessness, chest tightness, and coughing, particularly at night or in the early morning. These episodes are associated with widespread but variable airflow obstruction that is reversible either spontaneously, or with treatment.

Asthma

- Most common chronic condition in children
- #1 cause of school absenteeism
- Death rate up 50% from 1980 to 2000
- Death rate up 80% in people under 19
- Morbidity and mortality highly correlated with
 - Poverty, urban air quality, indoor allergens, lack of patient education, and inadequate medical care
- About 5000 deaths annually

Asthma

- Every day in the US, because of asthma:
 - 40,000 people miss school or work
 - 30,000 people have an asthma attack
 - 5,000 people visit the emergency room
 - 1,000 people are admitted to the hospital
 - 14 people die
- (Asthma and Allergy Foundation of America)

Asthma

- In 2000, 11 million reported having asthma attacks
- >5% of kids <18 reported an asthma attack
- In 1999, 2 million ER and 478,000 hospitalizations with asthma as the primary dx
- Mortality in Black males 3X that of white
- Mortality in Black females 2.5X that of white

Asthma

- Usually associated with airflow obstruction of variable severity.
- Airflow obstruction is usually reversible, either spontaneously, or with treatment
- The inflammation associated with asthma causes an increase in the baseline bronchial hyperresponsiveness to a variety of stimuli
- Clinical Diagnosis

Asthma Triggers

- Allergens
 - Dust mites, mold spores, animal dander, cockroaches, pollen, indoor and outdoor pollutants, irritants (smoke, perfumes, cleaning agents)
- Pharmacologic agents (ASA, beta-blockers)
- Physical triggers (exercise, cold air)
- Physiologic factors
 - Stress, GERD, viral and bacterial URI, rhinitis

Diagnostic Testing

- Peak expiratory flow (PEF)
 - Inexpensive
 - Patients can use at home
 - May be helpful for patients with severe disease to monitor their change from baseline every day
 - Not recommended for all patients with mild or moderate disease to use every day at home
 - Effort and technique dependent
 - Should not be used to make diagnosis of asthma

Diagnostic Testing

- Spirometry
 - Recommended to do spirometry pre- and post- use of an albuterol MDI to establish reversibility of airflow obstruction
 - $\geq 12\%$ reversibility or an increase in FEV1 of 200cc is considered significant
 - Obstructive pattern: reduced FEV1/FVC ratio
 - Restrictive pattern: reduced FVC with a normal FEV1/FVC ratio

Diagnostic Testing

- Spirometry
 - Can be used to identify reversible airway obstruction due to triggers
 - Can diagnose Exercise-induced asthma (EIA) or Exercise-induced bronchospasm (EIB) by measuring FEV1/FVC before exercise and immediately following exercise, then for 5-10 minute intervals over the next 20-30 minutes looking for post-exercise bronchoconstriction

Diagnostic Testing

- Spirometry
 - National Asthma Education and Prevention Program (NAEPP) recommends spirometry:
 - For initial assessment
 - Evaluation of response to treatment
 - Assessment of airway function at least every 1-2 years

Diagnostic Testing

- Methacholine challenge
 - Most common bronchoprovocative test in US
 - Patients breathe in increasing amounts of methacholine and perform spirometry after each dose
 - Increased airway hyperresponsiveness is established with a 20% or more decrease in FEV1 from baseline at a concentration $< 8\text{mg/dl}$
 - May miss some cases of exercise-induced asthma

Diagnostic testing

- Diagnostic trial of anti-inflammatory medication (preferably corticosteroids) or an inhaled bronchodilator
 - Especially helpful in very young children unable to cooperate with other diagnostic testing
 - There is no one single test or measure that can definitively be used to diagnose asthma in every patient

Goals of Asthma Treatment

- Control chronic and nocturnal symptoms
- Maintain normal activity, including exercise
- Prevent acute episodes of asthma
- Minimize ER visits and hospitalizations
- Minimize need for reliever medications
- Maintain near-normal pulmonary function
- Avoid adverse effects of asthma medications

Treatment of Asthma

- Global Initiative for Asthma (GINA) 6-point plan
 - Educate patients to develop a partnership in asthma management
 - Assess and monitor asthma severity with symptom reports and measures of lung function as much as possible
 - Avoid exposure to risk factors
 - Establish medication plans for chronic management in children and adults
 - Establish individual plans for managing exacerbations
 - Provide regular follow-up care

Written Action Plans

- Written action plans for patients to follow during exacerbations have been shown to:
 - (Cochrane review of 25 studies)
 - Decrease emergency department visits
 - Decrease hospitalizations
 - Improve lung function
 - Decrease mortality in patients presenting with an acute asthma exacerbation
 - NAEPP recommends a written action plan*

Pharmacotherapy

- Long-acting beta2-agonists (LABA)
 - Beta2-receptors are the predominant receptors in bronchial smooth muscle
 - Stimulate ATP-cAMP which leads to relaxation of bronchial smooth muscle and inhibition of release of mediators of immediate hypersensitivity
 - Inhibits release of mast cell mediators such as histamine, leukotrienes, and prostaglandin-D2
 - Beta1-receptors are predominant receptors in heart, but up to 10-50% can be beta2-receptors

Pharmacotherapy

- Long-acting beta2-agonists (LABA)
 - Salmeterol (Serevent)
 - Salmeterol with fluticasone (Advair)
 - Should only be used as an additional treatment when patients are not adequately controlled with inhaled corticosteroids
 - Should not be used as rescue medication
 - Can be used age 4 and above with a DPI
 - Deaths associated with inappropriate use as only medication for asthma

Pharmacotherapy

- Albuterol
 - Short-acting beta2-agonist
 - ATP to cAMP leads to relaxation of bronchial smooth muscle, inhibition of release of mediators of immediate hypersensitivity from cells, especially mast cells
 - Should be used prn not on a regular schedule
 - Prior to exercise or known exposure to triggers
 - Up to every 4 hours during acute exacerbation as part of a written action plan

Pharmacotherapy

- Inhaled Corticosteroids
 - Anti-inflammatory (but precise MOA not known)
 - Act locally in lungs
 - Some systemic absorption
 - Risks of possible growth retardation thought to be outweighed by benefits of controlling asthma
 - Not intended to be used as rescue medication
 - Benefits may not be fully realized for 1-2 weeks
 - Preferred treatment in persistent asthma

Pharmacotherapy

- Mast cell stabilizers (cromolyn/nedocromil)
 - Inhibits release of mediators from mast cells (degranulation) after exposure to specific antigens
 - Blocks Ca^{2+} ions from entering the mast cell
 - Safe for pediatrics (including infants)
 - Should be started 2-4 weeks before allergy season when symptoms are expected to be effective
 - Can be used before exercise (not as good as ICS)
 - Alternate med for persistent asthma

Pharmacotherapy

- Leukotriene receptor antagonists
 - Leukotriene-mediated effects include:
 - Airway edema
 - Smooth muscle contraction
 - Altered cellular activity associated with the inflammatory process
 - Receptors have been found in airway smooth muscle cells and macrophages and on other pro-inflammatory cells (including eosinophils and certain myeloid stem cells) and nasal mucosa

Pharmacotherapy

- Leukotriene receptor antagonists
 - No good long-term studies in pediatrics
 - Montelukast as young as 2; zafirlukast age 7
 - Alternate, but not preferred medication in persistent asthma and as addition to ICS
 - Showed a statistically significant, but modest improvement when used as primary medication

Pharmacotherapy

- Theophylline
 - Narrow therapeutic index/Maintain 5-20 mcg/mL
 - Variability in clearance leads to a range of doses that vary 4-fold in order to reach a therapeutic dose
 - Mechanism of action
 - Smooth muscle relaxation (bronchodilation)
 - Suppression of the response of the airways to stimuli
 - Increase force of contraction of diaphragmatic muscles
 - Interacts with many other drugs

Various severities of asthma

- Step-wise pharmacotherapy treatment program for varying severities of asthma
 - Mild Intermittent (Step 1)
 - Mild Persistent (Step 2)
 - Moderate Persistent (Step 3)
 - Severe Persistent (Step 4)
- Patient fits into the highest category that they meet one of the criteria for

Mild Intermittent Asthma

- Day time symptoms ≤ 2 times q week
- Night time symptoms ≤ 2 times q month
- PEF or FEV1 $\geq 80\%$ of predicted
- PEF variability $< 20\%$
 - PEF and FEV1 values are only for adults and for children over the age of 5

Mild Persistent Asthma

- Day time symptoms $> 2/\text{week}$, but $< 1/\text{day}$
- Night time symptoms < 1 night q week
- PEF or FEV1 $\geq 80\%$ of predicted
- PEF variability 20%-30%

Moderate Persistent Asthma

- Day time symptoms q day
- Night time symptoms > 1 night q week
- PEF or FEV1 60%-80% of predicted
- PEF variability $> 30\%$

Severe Persistent Asthma

- Day time symptoms: continual
- Night time symptoms: frequent
- PEF or FEV1 \leq 60% of predicted
- PEF variability $>$ 30%

Pharmacotherapy for Adults and Children Over the Age of 5 Years

- Step 1 (Mild intermittent asthma)
 - No daily medication needed
 - PRN short-acting bronchodilator (albuterol) MDI
 - Severe exacerbations may require systemic corticosteroids
 - Although the overall diagnosis is “mild intermittent” the exacerbations themselves can still be severe

Pharmacotherapy for Adults and Children Over the Age of 5 Years

- Step 2 (Mild persistent)
 - Preferred Treatment
 - Low-dose inhaled corticosteroid daily
 - Alternative Treatment (no particular order)
 - Cromolyn
 - Leukotriene receptor antagonist
 - Nedocromil
 - Sustained release theophylline to maintain a blood level of 5-15 mcg/mL

Pharmacotherapy for Adults and Children Over the Age of 5 Years

- Step 3 (Moderate persistent)
 - Preferred Treatment
 - Low-to-medium dose inhaled corticosteroids
 - WITH long-acting inhaled beta2-agonist
 - Alternative Treatment
 - Increase inhaled corticosteroids within the medium dose range
 - Add leukotriene receptor antagonist or theophylline to the inhaled corticosteroid

Pharmacotherapy for Adults and Children Over the Age of 5 Years

- Step 4 (Severe persistent)
 - Preferred Treatment
 - High-dose inhaled corticosteroids
 - AND long-acting inhaled beta2-agonists
 - AND (if needed) oral corticosteroids

Pharmacotherapy for Infants and Young Children (<5 years)

- Step 1 (mild intermittent)
 - No daily medication needed

Pharmacotherapy for Infants and Young Children (<5 years)

- Step 2 (mild persistent)
 - Preferred treatment
 - Low-dose inhaled corticosteroids
 - Alternative treatment
 - Cromolyn (nebulizer preferred)
 - OR leukotriene receptor antagonist

Pharmacotherapy for Infants and Young Children (<5 years)

- Step 3 (moderate persistent)
 - Preferred treatment
 - Low-dose inhaled corticosteroids and long-acting beta₂-agonist
 - OR Medium-dose inhaled corticosteroids
 - Alternative treatment
 - Low-dose inhaled corticosteroids with either:
 - Leukotriene receptor antagonist
 - OR theophylline

Pharmacotherapy for Infants and Young Children (<5 years)

- Step 4 (severe persistent)
 - Preferred treatment
 - High-dose inhaled corticosteroids
 - AND long-acting inhaled beta2-agonist
 - AND (if needed) Oral corticosteroids
 - For young children, inhaled medications should be given by nebulizer, dry powder inhaler (DPI), or MDI with a chamber/spacer

Acute Exacerbations

- Inhaled albuterol is the treatment of choice in absence of impending respiratory failure
- MDI with spacer as effective as nebulizer with equivalent doses
- Adding an antibiotic during an acute exacerbation is not recommended in the absence of evidence of an acute bacterial infection

Acute Exacerbations

- Beneficial
 - Inhaled atrovent added to beta2-agonists
 - High-dose inhaled corticosteroids
 - MDI with spacer as effective as nebulizer
 - Oxygen
 - Systemic steroids
- Likely to be beneficial
 - IV theophylline

Exercise-induced Bronchospasm

- Evaluate for underlying asthma and treat
- SABA are best pre-treatment
- Mast cell stabilizers less effective than SABA
- Anticholinergics less effective than mast cell stabilizers
- SABA + mast cell stabilizer not better than SABA alone

Question

- Which one of the following is true concerning control of mild persistent asthma in the pediatric population?
 - Cromolyn should not be used under age 5
 - Atrovent should be added if beta-agonists do not maintain control of asthma
 - LABA should be added if SABA is ineffective
 - SABA may be used q2h to maintain control
 - Initial treatment should be an inhaled anti-inflammatory such as ICS or cromolyn

Answer E

- Initial medications for chronic asthma should include an anti-inflammatory such as ICS or cromolyn. Cromolyn is safe for all pediatric age groups. Atrovent is useful in COPD, but very limited use in asthma. Albuterol should be used up to every 4 hours prn. Overuse of inhaled beta-agonists has been associated with an increased mortality rate.

Question

- It is estimated allergic rhinitis affects how many people in the US?
 - 20 million
 - 40 million
 - 50 million
 - 100 million
- Answer: B 40 million

Question

- Which one of the following statements concerning the association between allergic rhinitis and asthma is false?
 - Almost all patients with allergic asthma also have symptoms of rhinitis
 - About 1/3 of patients with allergic rhinitis also have asthma
 - Pharmacologic treatment for allergic rhinitis will not improve the symptoms of asthma
 - Patients with allergic rhinitis and patients with asthma exhibit peripheral eosinophilia and basophilia.

Answer: C

- Patients with asthma should have their allergic rhinitis treated
- People with asthma and allergic rhinitis who are treated for their allergic rhinitis have a significantly lower risk of subsequent asthma-related events than those not treated for allergic rhinitis.

Question

- Which one of the following findings on a nasal smear suggests a diagnosis of allergic rhinitis?
 - $> 10\%$ neutrophils
 - $> 10\%$ eosinophils
 - $< 10\%$ neutrophils
 - $> 10\%$ erythrocytes
- Answer: B $>10\%$ eosinophils

Question

- Which of the following statements is true?
 - An acceptable strategy for eliminating sedating effects of 1st-generation antihistamines and containing the cost of 2nd-generation is to use 2nd-generation in the AM and 1st-generation in the PM
 - In most states, patients taking 1st-generation are considered “under the influence of drugs.”
 - Mast cell stabilizers are becoming an excellent choice for children because of their ability to treat symptoms after they have started and their safety

Answer: B

- Patients taking 1st-generation antihistamines are considered “under the influence of drugs.” The sedating effects have been shown to carry over to the next day even when taken only at night and this type of chronic use is not recommended.
- Mast cell stabilizers should be started before symptoms develop, not after.

Questions?

